2 OVERVIEW OF STATUTORY AND REGULATORY REQUIREMENTS

Medical devices are classified by the FDA into one of three regulatory Classes: I, II, or III as required by the FD&C Act. The class of a device determines the level of regulatory control that applies to it. Medical gloves are in Class I (currently, Class I reserved). In addition, FDA has proposed that surgeon's gloves and patient examination gloves be reclassified into Class II.

Medical gloves are subject to general controls as follows:

- Establishment Registration,
- Device Listing,

- Premarket Notification [also known as 510(k) submission],
- Labeling,
- Quality Systems requirements, and
- Medical Device Reporting (MDR).

Regulations discussing these general controls are published in Title 21 of the United States (U.S.) Code of Federal Regulations (CFR). Applicable parts of these regulations and guidance on how to meet them are described herein.

REGISTRATION (21 CFR Part 807)

Who Must Register. All domestic and foreign medical glove manufacturers, contract manufacturers of finished gloves, specifications developers, contract sterilizers, initial domestic distributors (importers), repackers, and relabelers are required to register their establishment with FDA. To register, complete form FDA 2891, Initial Registration of Medical Device Establishment. You must use an original form -- **do not use a photocopy.** Forms can be obtained at FDA offices throughout the U.S. (please check your local telephone directory under Government) or by contacting the Division of Small Manufacturers Assistance (DSMA) by FAX at 301-443-8818 or Email at dsma@cdrh.fda.gov. Be sure to include a clearly printed return mailing address.

When domestic and foreign manufacturers register for the first time, they must also submit a device listing form. Requirements, such as listing, 510(k) submissions and medical device reporting are described below. If you have filed or plan to file a 510(k), you do not need to submit the registration and listing forms until after you receive your marketing clearance letter from FDA.

Where to Mail. Mail the completed registration form FDA 2891 to the following address:

Information Processing and Office Automation Branch (HFZ-307)
Center for Devices and Radiological Health
Food and Drug Administration
2098 Gaither Road
Rockville, Maryland 20850 USA
FAX 301-495-4660 (For registration problems only -- do not FAX the form.)

LISTING (21 CFR Part 807)

Who Must List. Domestic manufacturers, foreign manufacturers, repackers, or relabelers must list with FDA the type of device they market in the U.S. Also, specifications developers are required to list each type of medical glove if they distribute medical gloves. To list, complete form FDA 2892, "Device Listing," and **mail** it to the above address. Use an original form -- **do not use a photocopy and do not FAX the form to the FDA.**

(Information needed for Block #8, Classification Number, on form FDA 2892 can be located in Tables 3.1 and 3.2 under "Product Codes" in Chapter 3 of this guidance.)

Importer's Obligation. Initial distributors/importers have a listing obligation, but they do **not** satisfy it by completing form FDA 2892. Instead, initial distributors/importers should send a letter on their company letterhead to the above address.

The initial distributor's listing letter must state:

- the names and addresses of the foreign device manufacturers that supply the devices to the importer, and

- the devices being imported, their classification name, and FDA classification numbers.

Forms and Instructions. Blank copies of the establishment registration form FDA 2891, and the medical device listing form FDA 2892, along with the instruction booklet, are available from the Information Processing and Office Automation Branch at the above address or from:

Publications
DSMA (HFZ-220)
Food and Drug Administration
1350 Piccard Drive
Rockville, Maryland 20850 USA

Please request by FAX at 301-443-8818. (Please make sure your FAX number, name and address are in large clear print on your FAX requests so the forms can be mailed to you.)

Where to Mail. Do ***not*** mail completed registration or listing forms to DSMA. This will delay processing of the forms that you submit to FDA. Completed forms FDA 2891 and FDA 2892 should be mailed to the Information Processing and Office Automation Branch. After making a copy for your files, submit all pages of the original registration form and listing form to the Information Processing and Office Automation Branch, the same office and address shown under "Registration" on a previous page. Do ***not*** send photocopies or FAX copies. *Only the original forms will be accepted for processing.*

PREMARKET NOTIFICATION [510(k)] (21 CFR Part 807)

The following information is for your use in preparing a premarket notification [510(k)] for medical gloves. Although some of the information below may not be captured in the regulations, the suggestions represent FDA's position in rendering a substantial equivalence decision for a 510(k) for medical gloves.

What is a 510(k) Premarket Notification Submission. A 510(k) is a premarket application sent to the FDA documenting that the finished medical glove you wish to market is as safe and effective as a legally marketed medical glove that was, or is, on the U.S. market.

A premarket notification submission, also known as a 510(k) submission, ***must*** be submitted to FDA prior to marketing medical gloves as required by Section 510(k) of the FD&C Act. Upon receipt, FDA will send the manufacturer an acknowledgment letter which contains a unique document control number (i.e., **K** followed by **6** digits) that has been assigned to their 510(k) application. The acknowledgment letter with the 510(k) document control number (Attachment A in this chapter) is ***not*** clearance from FDA for the manufacturer to market the gloves. The manufacturer should not market or enter the gloves into the U.S. until a marketing clearance letter, also called an order or substantial equivalence letter, is received from FDA (Attachment B).

The premarket notification submitted to FDA must contain information that demonstrates that the glove is substantially equivalent to a medical glove that has been legally marketed in the U.S. which did not require a Premarket Approval Application (PMA). The submission should be adequate if it contains the data and information covered by the suggested 510(k) format outlined in Chapters 8 or 9. If the gloves conforms to a standard which has been recognized by the FDA, the standard becomes the basis for comparison.

Test data in 510(k) submissions should be the result of tests performed on finished medical gloves that were made by the same process as regular production medical gloves intended to be distributed. The water leak test data in the 510(k) submission should be from recently manufactured gloves and from gloves that have been aged for 3 to 12 months of real time aging or subjected to accelerated aging for 7 days at 70 degrees Centigrade as described in ASTM D standard 3578, D 3577 or D 5250, as appropriate, or an equivalent aging method. (In contrast, water leak testing for routine production is done on non-aged gloves.)

Who Must Submit a Premarket Notification. The following owners or operators must submit a 510(k) to the FDA:

- **Domestic manufacturers** -- manufacturers producing medical gloves within the U.S., or any Territory or possession of the U.S.

- **Specification developers** -- product developers that specify unique characteristics in design or production to a contract manufacturer. Such specifications must be documented per 21 CFR 820.181. Simply telling a contract manufacturer to produce gloves to the
- ASTM standard specification does not qualify you as a specification developer, because the standard is the baseline or minimum requirement.

- **Foreign manufacturers / exporters** or U.S. representatives of foreign manufacturers/ exporters introducing a device to the U.S. market, which can include distributors of imported medical devices; and

- **Relabelers / repackers** -- manufacturers that make significant labeling changes such as deletion or addition of cautions, warnings, contraindications or claims.

After being cleared for commercial distribution by the FDA, the specific glove covered by that 510(k) may be imported by any one or more U.S. distributor(s). Only one premarket notification [510(K)] is required for each glove type (such as powder free or powdered, colored, flavored, protein content, claim, etc.). It is the responsibility of the distributor to provide the correct 510(k) number to the FDA upon request by the Agency.

Overview of a 510(k) Submission. It is extremely important that you follow the guidance in this manual and 21 CFR Part 807 when preparing and submitting a 510(k) for medical gloves because the submission must meet requirements for applicant and device identification, safety, performance, labeling, identification of intended use, public release of non-confidential information under Freedom of Information, etc. Details are found in Chapters 2 through 9 of this manual.

Truthful and Accurate Statement. As required by 21 CFR 807.87(j), all 510(k) submitters must include a statement that all data submitted must be truthful and accurate. The following language in the statement cannot be altered or modified.

> I certify that, in my capacity as (*The Position Held in Company*) of (*Manufacturer's Name*), I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

The statement should be signed by a responsible person of the firm required to submit the premarket notification -- ***not*** by a consultant for the firm submitting the premarket notification (see chapter 7 for details.)

Indications for Use Statement. The 510(k) submission must include an "Indications for Use" page that contains the name of the device and the indications for use of the gloves as described in Chapter 7 of this manual.

The information, data and labeling claims in the entire 510(k) submission should support and agree with the Indications for Use statement.

How Do You Submit a Premarket Notification for Medical Gloves. There is no form for submitting a 510(k) for medical devices, only a detailed format to follow as listed in 21 CFR Part 807. However, due to the large number of 510(k) submissions for medical gloves, the use of a uniform format specifically intended for medical glove submissions will reduce submission errors and make processing by FDA more efficient. A copy of a recommended "format" is contained in Chapter 8, *Patient Examination Gloves.* Similarly, a recommended

format detailing the content of a 510(k) submission for surgeon's gloves is included in Chapter 9, *Surgeon's Gloves*.

Safe Medical Devices Act Summary or Statement. Persons who submit a 510(k) submission are required by the FD&C Act, as amended by the Safe Medical Devices Act of 1990 (SMDA 90), to provide to FDA as part of the 510(k) submission:

- a summary of 510(k) safety and effectiveness (S&E) information upon which the substantial equivalence determination is based, **or**

- a statement in the 510(k) submission that S&E information will be made available to interested persons upon request.

The requirements for the summary or statement are specific and detailed. See chapter 7 and 21 CFR §§807.92 and 807.93 for details and model language.

Where Do You Submit the 510(k). The **original** premarket notification submission and one copy should be sent by a method that **assures a return receipt as proof of delivery**. Send your 510(k) to the following address:

Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
1390 Piccard Drive
Rockville, Maryland 20850 USA

It is illegal to place a device into commercial distribution in the U.S. until you receive a letter from FDA stating that your device is substantially equivalent. Marketing the device prior to FDA clearance would render the device adulterated under §501(f)(1)(B) of the FD&C Act and subject to enforcement action by FDA.

FDA Requests Additional Information. After you submit your application, if FDA requests additional information by telephone, FAX, Email, or letter, you should:

- either submit the information within the requested time, or request an extension for submitting information and state the time needed to submit; and

- identify the additional information you are submitting with your company name and 510(k) number.

Modifications. Under the New 510(k) Paradigm, a manufacturer should refer to 21 CFR 807.81(a)(3) and the FDA guidance document entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device" at http://www.fda.gov/cdrh/ode/510kmod.html to decide if a device modification may be implemented without submission of a new 510(k). If a new 510(k) is needed for the modification and if the modification does not affect the intended use

of the device or alter the fundamental scientific technology of the device, then summary information that results from the design control process can serve as the basis for clearing the application.

"Special" 510(k). The Center for Devices and Radiological Health has developed an alternative method for obtaining clearance to market a modified version of an existing, legally marketed, device. This method of submission is called the Special 510(k), as discussed in the next paragraph. A properly prepared Special 510(k), which is accepted by FDA, will be reviewed within 30 days. If, for some reason, FDA does not accept the submission as a Special 510(k) (e.g., new indication for use, your certifications are not done, etc.), it will be converted to a Traditional 510(k)

A manufacturer who is intending to modify his/her own legally marketed device will conduct the risk analysis and the necessary verification and validation activities to demonstrate that the design outputs of the modifed device meet the design input requirements. Once the manufacturer has ensured the satisfactory completion of this process, a Special 510(k): Device Modification may be submitted. The Special 510(k) is explained in two guidance documents, "The New 510(k) Paradigm - Alternate Approaches to Demonstrating Substantial Equivalence in Premarket Notifications," at: http://www.fda.gov/cdrh/ode/parad510.html and its companion document which shows examples, "Frequently Asked Questions On The New 510(k) Paradigm," also on FDA's web site at: http://www.fda.gov/cdrh/ode/qanda510k.pdf.

A 510(k) application for a modification must be complete. Do ***not*** state that the necessary information is in another 510(k); instead, include all the necessary information in your submission. Also, the 510(k) should include appropriate supporting data to show that the manufacturer has considered what consequences and effects the change or modification or new use might have on the safety and effectiveness of the gloves, as described in 21 CFR 807.87(g).

The description of the modified gloves should include differences from the predicate gloves that could significantly affect safety and effectiveness. Provide any animal, engineering, design verification, bench, clinical, functional, in vitro, chemical resistance, and/or any other testing data that support the claims in your labeling for your modified gloves.

The requirements described above for a modification would be fulfilled if the applicant supplies the new information in another complete submission using the format described in Chapter 8, *Patient Examination Gloves*. Similarly, a suggested format detailing the content of a 510(k) submission for surgeon's gloves is included in Chapter 9, *Surgeon's Gloves*. Also, the applicant should reference the 510(k) number for the original gloves or accessory.

Transfer of Ownership of a 510(k)

A premarket notification [510(k)], like any other piece of property, may be bought, sold, or otherwise transferred. After a 510(k) substantial equivalence determination is issued to the

submitter by FDA, the FDA is not involved in subsequent transfer of ownership or questions of ownership of a 510(k). Consequently, the change of ownership is not submitted to the FDA.

Information documenting the transfer of ownership of a 510(k), including any legal transactions that transpired, should be maintained in the new owner's 510(k) files. Upon inspection of the firm or upon entry of glove shipments into the U.S., FDA may request a review of this documentation, and if the owner fails to provide such information, FDA may request the owner to submit a 510(k). Under these conditions the owner may not distribute the device until FDA clears the new submission.

The new owner of the transferred 510(k) should submit a new medical device listing, form FDA 2892, to FDA. The previous owner of the 510(k) should send:

1) a letter notifying FDA if they are now out of business, and

2) device listing forms deleting any listings for products no longer being marketed by that firm.

Please note that neither establishment registration nor medical device listing identifies the establishment with the 510(k) ownership. It is the responsibility of the new owner of the 510(k) to keep documentation proving ownership of the 510(k) in their files.

In order to avoid problems upon import of a device for which 510(k) ownership has been transferred, it is recommended that a copy of the key information about the ownership sale or transfer documentation accompany all shipments to the United States. It could be a simple, one-page document giving concise information detailing the transfer transaction.

THE NEW 510(k) PARADIGM

A 510(k) submission for a new glove or for a modification to an existing glove may be submitted according to the guidance titled, "*The New 510(k) Paradigm - Alternative Approaches to Demonstrating Substantial Equivalence in Premarket Notifications*," available on the World Wide Web at: http://www.fda.gov/cdrh/ode/parad510.pdf

LABELING

The FD&C Act defines a label as a "display of written, printed, or graphic matter upon the immediate container of any article" (i.e., glove dispenser box) (21 USC 321 (k)).

Labeling is a broader term defined by the FD&C Act as “all labels and other written, printed, or graphic matter” upon any article or any of its containers or wrappers; or

accompanying the article at any time while it is being held for sale after shipment or delivery for shipment in interstate commerce [21 USC 321 (m)]. Labeling includes some advertising, brochures and instructions, in any media such as printed text, software, encoded disks, or electronic transmissions.

Title 21 CFR Part 801 details labeling requirements for medical devices. Labeling requirements for latex medical gloves is currently found in §801.437. Proposed labeling requirements for medical gloves are located in proposed §801.440 and in Chapter 6 of this guidance. Any 510(k) submissions for medical gloves which do not include samples of the labeling will ***not*** be reviewed by FDA. Labeling does not need to be in final printed format; draft labeling may be submitted. The final labeling, however, should be consistent with draft labeling submitted in the 510(k) and should agree with your drawings for labeling and preprinted packaging in your Quality System device master record.

QUALITY SYSTEM REGULATION

Manufacturers of medical gloves are required to meet the current Quality System regulation for medical devices (21 CFR Part 820). The Quality System regulation requires that every finished medical glove manufacturer shall prepare and implement a quality assurance (QA) program or quality system that is appropriate to the specific type of glove being manufactured, and that meets the requirements of the QS regulation. A manufacturer's quality system must include:

- a management representative;
- adequate organization and sufficient trained personnel;
- documented quality system;
- documented review of QS by management with executive responsibility;
- design controls for surgeon's gloves, which, among other elements, ensure that design requirements address the intended use of the gloves, including the needs of the user and patient (pending the proposed reclassification of patient examination gloves into Class II, they will also be subject to design controls);
- specifications in the device master record for manufacturing materials, components, packaging, labeling, finished devices, processing, and quality control;
- change control of documents that are part of the device master record;
- approval or rejection of components such as raw latex and lubricating powders, in-process materials such as coagulant solutions, and finished gloves;
- proper cleaning and maintenance of equipment, control of environmental conditions such as temperature, humidity, and airborne particulates, and cleaning and maintenance of the facilities;
- the monitoring and control of manufacturing process specifications such as compounding, former cleaning, coagulant dipping, latex dipping, leaching, beading,

curing, post-cure washing, powdering, chlorination, neutralization, inspection or packaging;

- adequate and correct quality assurance checks (or acceptance criteria) to assure glove specifications are met (this includes assurance by real time or accelerated aging that claims are met when devices are delivered to the customer after reasonable and usual shipping, storage and handling, which means the glove will meet the intended use, including the needs of the user and patient);
- review of device history records (production records) before release of the lot;
- identification of quality system problems and specific glove defects, their causes, and actions necessary to correct them; and documentation of such corrective actions (CAPA);
- filing and investigating complaints from all sources with follow-up as necessary to correct any valid safety, performance, product, labeling or packaging problems; and
- periodic, documented quality system audits followed by corrective action as necessary.

Note that these quality system requirements are much more extensive than pass or fail inspections and air testing of finished gloves. They are intended to assure that continuing quality is incorporated into the gloves during manufacture, rather than by testing and removing defective gloves to achieve a quality product after manufacture. These requirements are discussed in more detail in Chapter 10, *Quality System Requirements as Applied to Medical Gloves,* with emphasis on latex processing.

MEDICAL DEVICE REPORTING

The purpose of the Medical Device Reporting (MDR) regulation, found in 21 CFR Part 803, is to provide the FDA with postmarketing information regarding adverse events occurring with the use of medical devices. Under the current provisions of the MDR regulation, device user facilities, domestic distributors, importers, and both domestic and foreign manufacturers of medical devices are subject to certain MDR requirements.

Manufacturers, importers, and user facilities must report adverse events when a device has or may have caused or contributed to a death or serious injury, and must establish and maintain adverse event files. They must submit to FDA specified follow-up and summary reports. Manufacturers and importers are also required to report certain device malfunctions to the FDA. Domestic distributors of medical devices in the U.S. are only required to maintain incident files and no longer have a reporting requirement.

Information gathered through medical device reporting assists FDA in protecting the public health by helping to assure that devices are not adulterated or misbranded, and are safe and effective for their intended use. FDA uses the MDR information to determine if user education programs are needed, whether product labeling needs improvement, whether devices need to be recalled, and during premarket submission reviews.

Manufacturers and user facilities will find a variety of guidance documents and other useful information on the CDRH home page at: http://www.fda.gov/cdrh/index.html. For additional information on MDR requirements, visit the Medical Device Reporting home page at: http://www.fda.gov/cdrh/mdr.html. Instructions for Completing the Medical Device Reporting Annual User Facility Report, Form FDA 3419 are at: http://www.fda.gov/cdrh/3419inst.html.

APPENDIX A - SUBSTANTIALLY EQUIVALENT LETTER

[510(k) HOLDER -- COMPANY NAME]
[C/O COMPANY REPRESENTATIVE, THIRD PARTY, OR CONSULTANT, (IF ANY)]
[COMPANY REPRESENTATIVE, THIRD PARTY, OR CONSULTANT ADDRESS]
[CITY, STATE, ZIP CODE]

Re: [510(k) NUMBER]
Regulatory Class:
Product Code:
Dated:
Received:

Dear [ADDRESSEE]:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-__. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

[DIVISION DIRECTOR]
[DIVISION DIRECTOR'S TITLE]
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

APPENDIX B - ACKNOWLEDGEMENT LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Food and Drug Administration
Center for Devices and
Radiological Health

Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

[Company Name]

510(k) Number: _____
Received: _____
Product: _____

The Center for Devices and Radiological Health (CDRH), Office of Device Evaluation (ODE), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in any future correspondence that relates to this submission. We will notify you when the processing of your premarket notification has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

On January 1, 1996, FDA began requiring that all 510(k) submitters provide on a separate page and clearly marked "Indication For Use" the indication for use of their device. If you have not included this information on a separate page in your submission, please complete the attached and amend your 510(k) as soon as possible. Also if you have not included your 510(k) Summary or 510(k) Statement, or your Truthful and Accurate Statement, please do so as soon as possible. There may be other regulations or requirements affecting your device such as Postmarket Surveillance (Section 522(a)(1) of the Act) and the Device Tracking regulation (21 CFR Part 821). Please contact the Division of Small Manufacturers Assistance (DSMA) at the telephone or web site below for more information.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the Document Mail Center will not be considered as part of your official premarket notification submission. Because of equipment and personnel limitations, we cannot accept telefaxed material as part of your official premarket notification submission, unless specifically requested of you by an FDA official. Any telefaxed material must be followed by a hard copy to the Document Mail Center (HFZ-401).

You should be familiar with the manual entitled, "Premarket Notification 510(k) Regulatory Requirements for Medical Devices" available from DSMA. If you have other procedural or policy questions, or want information on how to check on the status of your submission (after 90 days from the receipt date), please contact DSMA at (301) 443-6597 or its toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html or me at (301) 594-1190.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Staff
Office of Device Evaluation
Center for Devices and Radiological Health